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EXAMINER	
ART UNIT	PAPER NUMBER
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DATE MAILED: 12/03/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 6/24/96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☑ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449. (3)
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-58 are pending in the application.
   Of the above, claims 1-31 and 39-58 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 32-38 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. The sequence listing and amendments filed on 2/21/95 have been entered. Applicant's election without traverse of claims 32-38 in Paper No. 10 filed on 6/24/96 is acknowledged. Claims 1-31 and 39-58 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Applicant is required to cancel all non-elected claims in response to this Office Action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

16. Objections to the specification

a. Applicant is requested to update/insert the status of any copending and/or parent and/or foreign priority documents at paragraph 1 of the specification. Specifically, the status of the parent application (abandoned) should be inserted.

b. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

c. The drawings are objected to under 37 C.F.R. § 1.84 for the reasons set forth on the attached Substitute PTO Form 948.

d. The Brief Description of Figure 7 is objected to because it does not indicate that the figure includes an amino acid sequence. Amendment of the description to insert --and amino acid-- after "nucleotide" (p. 4, line 10), will overcome this objection.

e. The title of the invention is objected to because it is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is recommended: "Methods and Compositions for Detecting CDN Apoptosis-Modulating Proteins"

f. The Abstract of the Disclosure is objected to because it is not descriptive of the claimed invention. Correction is required. See M.P.E.P. § 608.01(b). Applicant is reminded of the proper content of an Abstract of the Disclosure.

> In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral antidiabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

g. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and *M.P.E.P.* § 608.01(l)(o). Correction of the following is required: (i) Claim 33 recites the limitation "lysing or permeabilizing" in line 5, "complex" in line 10, and "antibody-cdn complexes" in line 12. There is insufficient antecedent basis in the specification for these limitations in the claim. (ii) Claim 38 recites the limitation "T cells". There is insufficient antecedent basis in the specification for this limitation in the claim.

17. Rejections under 35 U.S.C. § 112

a. Claim 32-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 32 is directed to a composition comprising a monoclonal or polyclonal antibody which recognizes a CDN but is substantially unreactive with other members of the bcl family. The claim is indefinite in the recitation of "recognizes a CDN" because the precise meaning of "recognizes" and of the laboratory designation "CDN" is not clear; nor do these terms have a commonly accepted meaning in the art. Further, the meaning of "substantially unreactive" and the metes and bounds of "bcl family" cannot be ascertained from the disclosure.

Claims 33-38 are directed to a method of detecting the presence of a CDN protein in a biological sample. The claims are indefinite in the recitation of "a CDN protein" and "anti-cdns" and "CDN" for reasons *supra*.

In order to overcome these rejections, it is suggested that the claims be rewritten approximately as follows: --antibody which specifically binds to an apoptosis-associated CDN protein having the amino acid sequences of CDN-1, CDN-2, CDN-3, and the derivative proteins . . .--. Applicant is reminded that the appropriate SEQ ID NO: designations should be inserted after each reference in the claims to a CDN protein.

Finally, claim 32 is indefinite in the recitation of "composition" because only one element is recited, and a composition must recite two or more elements.

b. Claims 35, 37, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35 and 37 recite "nucleotide sequence." The phrase lacks antecedent basis in the claims. Claim 38 lacks antecedent basis in the claims for "The method according to claim 32" because the base claim does not recite a method.

c. Claims 33-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The method as claimed relies on immunologic detection of CDN protein in a cell sample which has been lysed or permeabilized. Such a method assumes that the protein is present intracellularly in sufficient amounts to be detected. However, the specification does not disclose whether the CDN protein accumulates intracellularly in biological samples (required by step b) or is secreted, or if the protein is in a form that is available to and bindable by antibodies made against recombinantly expressed CDN protein (the only enabled method of making anti-CDN protein antibodies). Rather, the specification provides indirect evidence of the existence of a CDN protein by showing that cells transfected with the cdn gene are resistant to apoptosis stimuli (see Examples 5 and 8). Thus, it is uncertain whether the CDN protein is detectable either in cell lysates or supernatants in a given cell sample. Assuming *arguendo* that the CDN protein is present intracellularly, it is uncertain whether it is present in sufficient quantity or in a form which is available for detectable binding to antibodies. Thus, in view of the limited guidance in the

specification, and the unpredictability associated with the presumed intracellular amount and availability of the protein, undue experimentation would be required to enable the method of detecting a CDN protein, including methods wherein the sample comprises T cells.

Further, detection of "nucleotide" sequences, as recited in claims 35 and 37, by antibodies raised against CDN protein is not enabled because one would not reasonably expect antibodies raised against a protein to react with the nucleic acid that encodes the protein.

Finally, with respect to claim 38, in view of the limited guidance in the specification and for reasons *supra*, it is unpredictable that T cells produce detectable quantities of CDN protein. Therefore, undue experimentation would be required to enable the method wherein the cell sample comprises T cells.

d. Claims 32-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies that bind to CDN proteins having the disclosed sequences, does not reasonably provide enablement for antibodies that bind to any CDN protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The disclosure is enabling for an antibody which specifically binds to an apoptosis-associated CDN protein having the amino acid sequences disclosed for CDN-1, CDN-2, CDN-3, and the disclosed variants thereof. The specification does not appear to specifically define the metes and bounds of CDN protein. As such the term cannot be considered to be limited to the specific CDN proteins disclosed in the specification. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable

identification of any other CDN proteins which meet the functional limitations of the claim. It cannot be predicted from the disclosure whether any and all CDN proteins will be detected by the antibodies. Therefore undue experimentation would be required to enable the claims.

18. Claims 33 and 38 are rejected for reasons set forth in the objections to the specification.

19. Prior art considerations

Claims directed to antibodies which bind to the specific apoptosis-associated CDN protein sequences disclosed in the specification appear to be free of the prior art.

20. No claim is allowed. Applicant is reminded that any amendments to the specification must not introduce new matter.

21. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray F. Ebert, Ph.D., whose telephone number is (703) 305-7023. The examiner normally can be reached Monday through Friday from 8:30 a.m. to 5:00 p.m., Eastern Standard Time.

Papers related to this application may be submitted to Group 1806 by facsimile transmission. Submissions by telefax must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The telefax number for this Group is (703) 308-4242.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

RFE

Ray F. Ebert, Ph.D.
Assistant Examiner

PHILLIP GAMBEL
PATENT EXAMINER
GROUP 1800

11/7/96

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